

How's My Dosing? Comparing Your Clinic's Maintenance Immunotherapy Doses to IT Practice Parameter Recommendations in One Convenient, Math-Free Step

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Abstract

The administration of allergen extracts at maintenance immunotherapy (IT) doses considered to be both effective and safe is an essential practice in allergy clinics. Although the establishment of appropriate dose ranges in IT vaccines remains a clinic-specific activity for many allergists in different geographic areas, treatment guidelines updated in the 2003 IT practice parameters¹ specified the quantities of standardized and non-standardized extracts likely to produce successful therapeutic outcomes with most patients. Comparisons of the maintenance doses used in allergy clinics with those reported in the practice parameters require several algebraic steps and a concentration-to-dose conversion based on the volume of injected vaccine. Multiple calculations are often required to account for differences in injection volume, extract concentrate strengths or allergen formulations within a single or group practice.

A simple, easy-to-use set of tables has been created to define the volumes of various extract concentrates required to be added to IT mixtures to deliver the recommended treatment doses cited in the practice parameters. Tables are included for specific (5.0 mL) or variable IT vial volumes and the three injection volumes used in most clinics (0.2 mL, 0.3 mL and 0.5 mL). The fractional volume tables can be revised easily to accommodate any IT vial volume-injection volume combination. Tables are constructed with columns defining the extract category, concentrate strength, target dose ranges and the resulting volumes or percentages needed to produce doses at the lower limit, upper limit and middle of each range.

Using these tables alone (no additional calculations required), allergy professionals can quickly determine the numbers and strengths of extracts that can be combined into a treatment mixture at the various dose levels, facilitating the selection of extract combinations that are most appropriate for their patients.

¹ LI JT, Lockey RF, Bernstein IL, Portnoy JM and Nicklas RA, eds. Allergen immunotherapy: A practice parameter. Ann Allergy Asthma Immunol 2003; 90 (1): 1-40.

IT Dose Conversions

Effective maintenance doses ranges published in the 2003 IT practice parameters included both standardized and non-standardized extracts. Non-standardized dose targets (0.5 mL injection volumes) were identical in w/v terms regardless of extract type or concentrate strength. Differences in PNU content at similar w/v strengths were not considered significant but may be important for some extracts. Standardized dose targets were similar for cat, dust mites and northern pasture grasses (1,000-4,000 BAU or AU). Bermuda grass targets were not specified and are listed as proportional to concentrate strengths by this author for use in patients possessing Bermuda sensitivities similar to those to the northern grasses.

The resulting IT dose ranges are tabulated below.

| Extract/Concentrate Strength | | Target dose range |
|---|-----------------------------------|-------------------|
| Category | Concentrate | |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 1:50-1:250 w/v |
| | 1:20 w/v | 1:50-1:250 w/v |
| Short ragweed | 1:10-1:20 w/v 200-400 AgE U/mL | 6-12 AgE U |
| Cat | 10,000 BAU/mL | 1,000-3,000 BAU |
| Dust mites | 10,000 AU/mL | 500-2,000 AU |
| Northern grasses | 100,000 BAU/mL | 1,000-4,000 BAU |
| Bermuda | 10,000 BAU/mL | 100-400 BAU |

To deliver the above doses in IT vaccines, 3 variables are involved: total volume of vaccine vials, final component concentrations in the maintenance vial, and injection volume. Using a common formula (conservation of mass, $V_1C_1 = V_2C_2$) or algebraic conversion (dilution factor or fractional volume), the volumes of each component required to achieve these target doses can be calculated for each allergen at the specific volumes employed for mixing and injection. The tables provided in this presentation have been created to eliminate the need for clinicians or mixing technicians to perform these calculations. These 6 tables represent the vaccine volumes (5.0 mL or variable) and injection volumes (0.2 mL, 0.3 mL and 0.5 mL) used in most allergy clinics.

0.5 mL Injections

The practice parameter recommendation for non-standardized and standardized extracts were based on a 0.5 mL injection volume. Extract volumes needed to match the target doses for effective treatment were determined at the lower limit (Min), upper limit (Max) and middle (Mid) of each range, and are tabulated below for both 5.0 mL (top) and variable (bottom) IT vial volumes administered at 0.5 mL injection volumes.

5.0 mL IT vial volumes 0.5 mL injection volumes

| Extract/Concentrate Strength | | mL of concentrate needed per vial | | |
|---|----------------|-----------------------------------|------|------|
| Category | Concentrate | Min | Mid | Max |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 0.20 | 0.60 | 1.00 |
| | 1:20 w/v | 0.40 | 1.20 | 2.00 |
| Short ragweed | 200 AgE U/mL | 0.30 | 0.45 | 0.60 |
| Cat | 10,000 BAU/mL | 1.00 | 2.00 | 3.00 |
| Dust mites | 10,000 AU/mL | 0.50 | 1.25 | 2.00 |
| Northern grasses | 100,000 BAU/mL | 0.10 | 0.25 | 0.40 |
| Bermuda | 10,000 BAU/mL | 0.10 | 0.25 | 0.40 |

Variable IT vial volumes 0.5 mL injection volumes

| Extract/Concentrate Strength | | % of vial volume | | |
|---|----------------|------------------|-----|-----|
| Category | Concentrate | Min | Mid | Max |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 4 | 12 | 20 |
| | 1:20 w/v | 8 | 24 | 40 |
| Short ragweed | 200 AgE U/mL | 6 | 9 | 12 |
| Cat | 10,000 BAU/mL | 20 | 40 | 60 |
| Dust mites | 10,000 AU/mL | 10 | 25 | 40 |
| Northern grasses | 100,000 BAU/mL | 2 | 5 | 8 |
| Bermuda | 10,000 BAU/mL | 2 | 5 | 8 |

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0.3 mL Injections

The use of 0.3 mL injection volumes (vs. 0.5 mL) requires significant (67%) increases in extract concentrate volumes to reach the same target doses. These differences reduce the number of allergens that can be included in maintenance IT vials and may result in higher glycerin levels in these mixtures.

5.0 mL IT vial volumes 0.3 mL injection volumes

| Extract/Concentrate Strength | | mL of concentrate needed per vial | | |
|---|----------------|-----------------------------------|------|------|
| Category | Concentrate | Min | Mid | Max |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 0.33 | 1.00 | 1.67 |
| | 1:20 w/v | 0.67 | 2.00 | 3.34 |
| Short ragweed | 200 AgE U/mL | 0.50 | 0.75 | 1.00 |
| Cat | 10,000 BAU/mL | 1.67 | 3.34 | 5.00 |
| Dust mites | 10,000 AU/mL | 0.83 | 2.09 | 3.34 |
| Northern grasses | 100,000 BAU/mL | 0.17 | 0.43 | 0.68 |
| Bermuda | 10,000 BAU/mL | 0.17 | 0.43 | 0.68 |

Variable IT vial volumes 0.3 mL injection volumes

| Extract/Concentrate Strength | | % of vial volume | | |
|---|----------------|------------------|------|------|
| Category | Concentrate | Min | Mid | Max |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 6.7 | 20 | 33.4 |
| | 1:20 w/v | 13.4 | 40 | 66.8 |
| Short ragweed | 200 AgE U/mL | 10 | 15 | 20 |
| Cat | 10,000 BAU/mL | 33.4 | 66.8 | 100 |
| Dust mites | 10,000 AU/mL | 16.7 | 41.7 | 66.8 |
| Northern grasses | 100,000 BAU/mL | 3.4 | 8.5 | 13.6 |
| Bermuda | 10,000 BAU/mL | 3.4 | 8.5 | 13.6 |

0.2 mL Injections

With 0.2 mL injection volumes, even higher increases in component volumes are required to achieve target doses (250% or 2.5X vs. 0.5 mL injections). Many of these doses are difficult or impractical to include in maintenance IT vials, and several maximum doses are not reachable (NR) with a 0.2 mL injection volume.

5.0 mL IT vial volumes 0.2 mL injection volumes

| Extract/Concentrate Strength | | mL of concentrate needed per vial | | |
|---|----------------|-----------------------------------|------|------|
| Category | Concentrate | Min | Mid | Max |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 0.50 | 1.50 | 2.50 |
| | 1:20 w/v | 1.00 | 3.00 | 5.00 |
| Short ragweed | 200 AgE U/mL | 0.75 | 1.13 | 1.50 |
| Cat | 10,000 BAU/mL | 2.50 | 5.00 | NR |
| Dust mites | 10,000 AU/mL | 1.25 | 3.13 | 5.00 |
| Northern grasses | 100,000 BAU/mL | 0.25 | 0.63 | 1.00 |
| Bermuda | 10,000 BAU/mL | 0.25 | 0.63 | 1.00 |

Variable IT vial volumes 0.2 mL injection volumes

| Extract/Concentrate Strength | | % of vial volume | | |
|---|----------------|------------------|------|-----|
| Category | Concentrate | Min | Mid | Max |
| Pollens, Molds, Inhalants, Animals, Insects | 1:10 w/v | 10 | 30 | 50 |
| | 1:20 w/v | 20 | 60 | 100 |
| Short ragweed | 200 AgE U/mL | 15 | 22.5 | 30 |
| Cat | 10,000 BAU/mL | 50 | 100 | NR |
| Dust mites | 10,000 AU/mL | 25 | 62.5 | 100 |
| Northern grasses | 100,000 BAU/mL | 5 | 12.5 | 20 |
| Bermuda | 10,000 BAU/mL | 5 | 12.5 | 20 |

Applications

Using the Min, Mid and/or Max columns of each table, the numbers and types of extracts that can be combined into IT vaccines are determined simply by adding the volumes from the columns corresponding to the desired doses, up to the total IT vial volume.

For example, clinics using 5.0 mL vial volumes and 0.5 mL injection volumes can reach Max doses with up to 5 1:10 w/v non-standardized extracts (1.0 mL each) and Min doses with up to 25 extracts at this strength (0.2 mL each).

Mixtures containing target levels of both non-standardized and standardized allergens are feasible with 0.5 mL injections, such as Mid doses of cat (2.0 mL), grasses (0.25 mL each) and dust mite (1.25 mL) with Min doses of 3-5 non-standardized products.

Many more extract combinations are possible with 0.5 mL injections compared to 0.2-0.3 mL treatments. With knowledge of extract compatibilities, IT vaccines can be formulated into a minimal number of maintenance vials for individual patients. Allergens at these target strengths are also more likely to remain stable during storage at 2-8°C and short-term exposures at room temperature (20-25°C).

Non-standardized extracts at 1:10-1:20 w/v strengths obtained from different allergen manufacturers may vary in PNU content and allergenic potency. Check with your extract provider to determine the levels of non-standardized extracts recommended for inclusion in IT vaccines.

Conclusions

The maintenance IT dose tables presented here provide clinicians a convenient and math-free guide for comparing their current doses to practice parameter recommendations. The numbers and types of extracts that can be combined in maintenance vials at these target doses are assessed easily by adding the volumes from the Min, Mid or Max dose columns of the appropriate tables. Informed dosing decisions can then be made for patients presenting with a wide range of allergen specificities and sensitivities.